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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
10/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/553,869	LORENTSEN ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *12 and 18-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 13-17* is/are rejected.

7)☒ Claim(s) *1-11 and 13-17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment of June 13, 2008, in response to the Action of January 16, 2008, is acknowledged. It is acknowledged that Claims 1-11 and 13-17 have been amended. Claims 1-39 are pending. Claims 12 and 18-39 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-11 and 13-17 are hereby reexamined.

Specification-Objections

Objection to the specification, for disclosing conflicting information regarding the structure of GrB-H6, is maintained. In support of their request that said objection be withdrawn, Applicants provide the following arguments.

> "For pro-IEGR-GrB-H6 (SEQ ID NO: 1), the first seven amino acids correspond to the Fxa recognition sequence, MGSIEGR (see top of page 32). Amino acid 8 for SEQ ID NO. 1 corresponds to Ile21 in Granzyme B (lie 16 in chymotrypsin numbering) (see Specification, top of page 32). SEQ ID NO. 1 correctly identifies the position of Tyr247.
>
> The three amino acids prior to the His tag are a part of the disclosed T7 cloning vector in which the His tag was cloned. Specifically, they correspond to restriction sites, including EcoR1 site. (see page 33, second paragraph). Page 13 of the specification explains that one of skill in the art would recognize Granzyme B protease variants where one or more amino acid residues are added, or deleted or conservative variations. Thus, with regard to the above discrepancies, the sequences are not conflicting and are fully supported by the disclosure.
>
> The applicants have amended the specification at the beginning of Example 1, on the top of page 32, to reflect that the Granzyme B sequence terminates with Tyr247. This correction adds no new matter as the Granzyme B sequence ending with Tyr247 was disclosed and fully supported throughout the original sequence listing (SEQ ID NO: 1, as one example)."

These arguments are, or are not, found to be persuasive for the following reasons.

It is acknowledged that (i) the first seven amino acids of SEQ ID NO: 1, MGSIEGR, corresponds to the Fxa recognition sequence and (ii) residues 235-243 of SEQ ID NO: 1 represent the encoded EcoRI restriction site and his-tag. However, SEQ ID NO: 1 does not contain an Ile21 residue or a Tyr247 residue. It is noted that reference to an amino acid by

residue number, without reference to a specific sequence, is indefinite. Moreover, Applicants' argument fails to clarify the sequence of the constructs named "GrB-H6" or "GrB".

Claims-Objections

Objection to Claims 1-11 and 13-17 for reciting non-elected subject matter is maintained. Applicants are reminded that the elected invention is directed to a method of cleaving a fusion protein using a human granzyme B enzyme, wherein the fusion protein comprises the cleavage motif IEAD; see the Action of January 16, 2008, page 2, paragraph 1, especially lines 3-7.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of Claim 5 as indefinite for failing to define P1', P2' or P3' is maintained. In support of their request that said rejection be withdrawn, Applicants argue that pages 8-9 of the specification define that residues P1', P2' or P3' may be any amino acid. This argument is not found to be persuasive. Said pages merely discuss the controversy over whether granzyme B will cleave a motif regardless of the amino acid residues at positions P1', P2' or P3'. Moreover, the specification, page 61, teaches that "GrB-H6 C228F" is better at cleaving IEPDEG than IEPDEP, demonstrating that the amino acid residue, at least at position P2', does affect cleavage. Thus, rejection of Claim 5 as indefinite for failing to define P1', P2' or P3' is maintained.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 1-11 and 13-17 under 35 U.S.C. 112, first paragraph/lack of enablement, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) The invention does not encompass "any protein having any structure to cleave a fusion protein" as asserted by the Examiner (Office Action, p. 8). The invention encompasses the use of Granzyme B only, which is distinct from other proteases. The specification defines Granzyme B: "Granzymes are granule-stored serine proteases that are implicated in T cell and natural killer cell-mediated cytotoxic defense reactions after target cell recognition and Granzyme B is one type of granzyme, and upon target cell contact it is directionally exocytosed and enters target cells (pg 7) and "Human Granzyme B protease occurs in most human tissues where its biological function is well known" (pg 8).

(B) The specification describes human, mouse, and rat Granzyme B sequences. The mouse and rat sequences have been published and it would not be undue experimentation for one of skill to use known Granzyme B sequences.

(C) The sequence listing discloses eight Granzyme B variants with modification of residues 4-7 and/or 228, while the Examples provide a plethora of variants (pg 32-33 and 39-4). In addition, over twenty cleavage sites were specifically disclosed in the specification (p. 10) and in the original claim 3 and 20.

(D) The invention comprises discrete amino acid substitutions, not protein domain swapping. Such simple amino acid substitutions would not result in unpredictable protein structure or function.

(E) The filed disclosure (A) provides sufficient teaching of a specific Granzyme B protease and Granzyme B sequence variants experimentally exhibiting protease activity as described immediately above. (See pgs. 10, 32, 33, 39, 40, 56, and 61, SEQ ID NOS: 1-8). The claims do not encompass 'any enzyme' as alleged in the Office Action. The disclosure provides (B) specific amino acids that can be modified to improve cleavage activity. (See p. 61). The disclosure (C) outlines the impact of protein modifications and the tolerance of enzyme cleavage activity throughout Examples 3, 4, 6 & 8. The specification and claims provide (D) specific amino acid cleavage sites (over 20) (see, e.g., p. 10) as well as the patterns of amino acid cleavage sites (see pp. 8-10), thus the claimed cleavage motifs are within scope of the disclosure. Again, (E) the above variants contain multiple amino acid substitutions and yet maintain cleavage activity (Example 8). (F) The plethora of cleavage motif modifications coupled with their continued activity provides sufficient teachings to enable one of skill in the art to predict cleavage motif variations and their tolerance for continued activity. Similar to E and F above, the (G) vast number of modified Granzyme variants would permit one of skill to modify the cleavage motif or residues with an expectation of obtaining the desired function (e.g. cleavage). (H): Based on the dozens of variants and the disclosure of experimental Examples (specific pages cites above), Applicants have provided sufficient guidance to enable one of skill in the art to practice a method for preparing fusion proteins via the cleavage of a Granzyme B site with a Granzyme B protease.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: The full scope of the recited invention encompasses a method for cleaving any fusion protein using any protein having any protease activity of any Granzyme B, wherein

the fusion protein comprises any motif that can be cleaved by any protein having any protease activity of any Granzyme B. Thus, full scope of the recited invention fails to provide any structural limitations for either the "any protein having any protease activity of any Granzyme B" or the "any motif that can be cleaved by any protein having any protease activity of any Granzyme B".

Applicants' argument that the invention encompasses "the use of Granzyme B only, which is distinct from other proteases, that Granzymes are granule-stored serine proteases that are implicated in T cell and natural killer cell-mediated cytotoxic defense reactions after target cell recognition, that Granzyme B is one type of granzyme, and upon target cell contact it is directionally exocytosed and enters target cells, and human Granzyme B protease occurs in most human tissues where its biological function is well known" also fails to provide any structural limitations for either the proteases or cleavage motifs encompassed. In addition said argument provides little if any functional limitation for the proteases: "implicated in T cell and natural killer cell-mediated cytotoxic defense" and "Granzyme B is one type of granzymes, and upon target cell contact it is directionally exocytosed and enters target cells, and human Granzyme B protease occurs in most human tissues where its biological function is well known".

For the instant invention to be enabled, the skilled artisan must know the structure and cleavage specificity for the encompassed Granzyme B proteases.

(B) Reply: The instant claims are not limited to the use of endogenous human, mouse, and rat Granzyme B sequences. The claims encompass the use of any protein having any protease activity of any Granzyme B.

(C) Reply: It is acknowledged that the sequence listing discloses eight Granzyme B variants comprising substitutions at one or more of five residues, while the specification, pages 32-33, describes the making of said eight variants. The specification, pages 39-40, asserts that two of said variants are self-activating. None of said pages disclose cleavage of a fusion protein with the eight Granzyme B variants. Moreover, even if said pages did disclose cleavage of a fusion protein with the eight Granzyme B variants, which they do not, disclosure of eight Granzyme B variants comprising substitutions at one or more of five residues of a 243 amino acid protein is not sufficient to teach the artisan how to make and use any protein having any structure and having any protease activity of any Granzyme B.

It is acknowledged that the specification at page 10 discloses what was taught in the prior art (Casciola-Rosen et al, 1999); 24 motifs that are cleaved by human Granzyme B. However, as explained above, the instant claims are not limited to use of human Granzyme B nor to use of said 24 motifs.

(D) Reply: The claims are not limited to use of Granzyme B variants comprising discrete amino acid substitutions. The claims encompass the use of any protein having any structure and having any protease activity of any Granzyme B.

(E) Reply: Regarding Applicants' assertion that the disclosure provides sufficient teaching of a specific Granzyme B protease and Granzyme B sequence variants experimentally exhibiting protease activity: as explained in (A) above the claims are not limited to the specific Granzyme B protease and Granzyme B sequence variants taught at pages 32, 33, 39, and 40. It is acknowledged that page 56 teaches that a construct named "GrB-H6" cleaves the motif "IEPD", while page 61 teaches that a construct named "GrB-H6 C228F" also cleaves the motif "IEPD".

However, the Examiner fails to find in the specification or sequence listing the structure of "GrB-H6" or "GrB-H6 C228F". Therefore, the disclosure fails to enable the skilled artisan to make and use said constructs.

Regarding Applicants' assertion that the disclosure provides specific amino acids that can be modified to *improve* cleavage activity (pg 61): it is acknowledged that page 61 teaches that "GrB-H6 C228F" is better at cleaving IEPDEG than IEPDEP. However said teaching does not enable the skilled artisan make and use the full scope of the invention (see (A), above).

Regarding Applicants' assertion that the disclosure outlines the impact of protein modifications and the tolerance of enzyme cleavage activity, see (A, C & D) above.

Because the claims encompass use of any protein having any protease activity of any Granzyme B, the skilled artisan would believe that, more likely than not, the 24 cleavage motifs disclosed by Casciola-Rosen et al, 1999 do not encompass all motifs cleaved by any protein having any protease activity of any Granzyme B.

Regarding Applicants' assertion that the above variants contain multiple amino acid substitutions and yet maintain cleavage activity, see (C) above.

Regarding Applicants' assertion that the plethora of cleavage motif modifications coupled with their continued activity provides sufficient teachings to enable one of skill in the art to predict cleavage motif variations and their tolerance for continued activity: it is acknowledged that the page 61 teaches that "GrB-H6 C228F" is better at cleaving IEPDEG than IEPDEP. However said teaching does not enable the skilled artisan make and use the full scope of the invention (see (A), above).

Regarding Applicants' assertion that the vast number of modified Granzyme variants would permit one of skill to modify the cleavage motif or residues with an expectation of obtaining the desired function (e.g. cleavage): to make and test the encompassed "vast number of modified Granzyme variants" for cleavage of any peptide motif clearly represents undue experimentation.

For these reasons and those explained in the prior action, rejection of Claims 1-11 and 13-17 under 35 U.S.C. 112, first paragraph/lack of enablement, is maintained.

Claims 7 and 8 are further rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for producing authentic somatotrophin, glucagon, insulin, interferon, or granzyme B by cleaving a fusion protein comprising said proteins with granzyme B. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Written Description

Rejection of Claims 1-11 and 13-17 under 35 U.S.C. 112, first paragraph/written description, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the same arguments presented above for the lack of enablement rejection. These arguments are not found to be persuasive for the reasons explained above.

Further rejection of Claims 4 and 5 under 35 U.S.C. 112, first paragraph/written description, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the argument that the specification

discloses that positions P1'-P4' can be any amino acid residue (pg 8-9). Said pages merely discuss the controversy over whether granzyme B will cleave a motif regardless of the amino acid residues at positions P1', P2' or P3'. Moreover, the specification, page 61, teaches that "GrB-H6 C228F" is better at cleaving IEPDEG than IEPDEP, demonstrating that the amino acid residue, at least at position P2', does affect cleavage. Thus, rejection of Claims 4 and 5 under 35 U.S.C. 112, first paragraph/written description, is maintained.

Claims 7 and 8 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 7 and 8 are directed to a genus of methods for producing authentic somatotrophin, glucagon, insulin, interferon, or granzyme B by cleaving a fusion protein comprising said proteins with granzyme B. The specification teaches no such methods. Given this lack of description of representative species encompassed by the genera of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 9-11, 16, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Harris et al, 1998. Harris et al teach a method of making a protein of interest, which is a linker+residues 198-406 of the pIII coat protein of M13 bacteriophage. Said method comprises incubating a fusion protein comprising, from the N-terminal to C-terminal, a His-tag fusion partner, a granzyme B cleavage motif of IXPDXX where X is any amino acid, and the protein of interest (pg 27365, parg 12) followed by contacting said fusion protein with granzyme B (pg 27366, parg 3; pg 27369, parg 2; Fig 3; Table IV), wherein the fusion protein is immobilized on Ni/nitrilotriacetic acid resin. For Harris et al, the desired polypeptide to be produced is a linker+residues 198-406 of the pIII coat protein of M13 bacteriophage; production of said polypeptide reflects cleavage by granzyme B. Therefore, Claims 1-4, 9-11, 16, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Harris et al, 1998.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of Claims 1-3, 6, 9-11, and 13-15 under 35 U.S.C. 103(a), as being unpatentable over Johnsen et al, 2000 in view of Harris et al, 1998 (IDS) and further in view of Pharmacia, Inc, 1986, is withdrawn. The rejection of Claim 4 under 35 U.S.C. 103(a) as being unpatentable over the combination of Johnsen et al, 2000 and Harris et al, 1998 in view of Parenti et al, 1993, is withdrawn. The rejection of Claim 5 under 35 U.S.C. 103(a) as being unpatentable over the combination of Johnsen et al, 2000 and Harris et al, 1998 in view of

Martin et al, 2000, is withdrawn. The rejection of Claim 7 under 35 U.S.C. 103(a) as being unpatentable over Boyer et al, 1992 in view of Harris et al, 1998, is withdrawn. The rejection of Claim 8 under 35 U.S.C. 103(a) as being unpatentable over Medabalimi, 2000 in view of Harris et al, 1998, is withdrawn. The rejection of Claims 16 and 17 under 35 U.S.C. 103(a) as being unpatentable over the combination of Johnsen et al, 2000 and Harris et al, 1998 in view of Braun et al, 1999, is withdrawn.

Claims 1-4, 9-11, 16, and 17 are herein rejected under 35 U.S.C. 103(a) as being unpatentable over Azad et al, 1994 in view of Harris et al, 1998. Azad et al teach a GST-nef27 fusion protein (pg 651, pargs 2-3). Azad et al does not teach a GST-granzyme B cleavage motif-nef27 fusion protein or using said fusion protein to produce nef27. As taught by Azad et al nef27 contains Met-Gly at the N-terminus (pg 651, parg 2; encoded by ATG-GGT). It would have been obvious to a person of ordinary skill in the art to modify the fusion protein of Azad et al to incorporate the motif IEAD, as taught by Harris et al (Fig 5D) between the GST fusion partner and nef27 and then generate nef27 by cleaving the fusion protein with granzyme B. Motivation to do so derives from the desire to produce nef27, which is critical for development of AIDS (Azad et al; Abstract). It would also be obvious to adapt the fusion protein rendered obvious by the above teachings to replace the GST fusion partner with a 6X-His fusion partner. Motivation to do so derives from the desire to use Ni/nitrilotriacetic acid resin for purification of the fusion protein, as taught by Harris et al (pg 27366, parg 3). The expectation of success is high, as the making and cleaving of fusion proteins is well-known in the art. Therefore, Claims 1-4, 9-11, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Azad et al, 1994 in view of Harris et al, 1998.

Claims 1-6, 9-11, 16, and 17 are herein rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Azad et al, 1994 and Harris et al, 1998 in view of Boutin et al, 1997. The teachings of Azad et al and Harris et al are described above. Said combination does not teach preparing a protein of interest by providing a fusion protein comprising, from the N-terminal to C-terminal, a fusion partner, a granzyme B cleavage motif, and the protein of interest followed by contacting said fusion protein with granzyme B, wherein the granzyme B cleavage motif comprises D or E at P4' as part of the protein of interest, or wherein the protein of interest is an enzyme. Boutin et al teach that, like nef27, essentially all proteins that become myristoylated begin with Met-Gly at the N-terminus (Table 3), including the enzyme calcineurin B, which has E at P4' (Table 3A). It would have been obvious to a person of ordinary skill in the art to modify the fusion protein rendered obvious by the combination of Azad et al and Harris et al, such that the nef27 protein is substituted with calcineurin B. Motivation to do so derives from the desire to produce calcineurin B, a calcium-dependent phosphatase. The expectation of success is high, as the making and cleaving of fusion proteins is well-known in the art. Therefore, Claims 1-6 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Azad et al, 1994 and Harris et al, 1998 in view of Boutin et al, 1997.

Claims 1-4, 9-11, and 13-15 are herein rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Azad et al, 1994 and Harris et al, 1998 in view of Sigma Inc, 1998. The teachings of Azad et al and Harris et al are described above. Said combination does not teach a method wherein the granzyme B is immobilized. However, the use of immobilized proteases for generating a polypeptide from a fusion protein is well-known in the art; see, for example Sigma, Inc. In addition, it was well-known that proteins can be

immobilized via the N-terminus, the C-terminus, or lysine residues (Pharmacia, Inc). It would have been obvious to a person of ordinary skill in the art to modify the method of rendered obvious by the combination of Azad et al and Harris et al to used immobilized granzyme B. Motivation to do so derives from the desire to circumvent the need to remove granzyme B from the generated polypeptide. The expectation of success is high, as the use of immobilized proteases for cleaving fusion proteins was well-known in the art. Therefore, Claims 1-4, 9-11, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Azad et al, 1994 and Harris et al, 1998 in view of Sigma, Inc 1998.

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652